PATENT COOPERATION TREATY

From the:
INTERNATIONAL SEARCHING AUTHORITY

To:

Davies Collison Cave
Level 15
1 Nicholson Street
MELBOURNE VIC 3000

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	18 AUG 2005
Applicant's or agent's file reference 12630510	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2005/000966	30 June 2005	2 July 2004

International Patent Classification (IPC) or both national classification and IPC
Int. Cl. [7] C07K 1/22, C07K 17/06, G01N 33/547

Applicant
BIO-LAYER PTY LTD et al

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [X] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU
AUSTRALIAN PATENT OFFICE
PO BOX 200, WODEN ACT 2606, AUSTRALIA
E-mail address: pct@ipaustralia.gov.au
Facsimile No. (02) 6285 3929

Authorized Officer
R. OSBORNE
Telephone No. (02) 6283 2404

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2005/000966

Box No. I Basis of the opinion

1. With regard to the **language,** this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2005/000966

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	**7-9, 13-19, 22-24, 28-29**	**YES**
	Claims	**1-6, 10-12, 20-21, 25-27**	**NO**
Inventive step (IS)	Claims	**7-8, 13-16, 24, 28-29**	**YES**
	Claims	**1-6, 9-12, 17-23, 25-27**	**NO**
Industrial applicability (IA)	Claims	**1-29**	**YES**
	Claims		**NO**

2. Citations and explanations:

D1: US 6013170 A (Meade) 11.01.2000

D2:US 2003/0003223 A1 (Mores *et al.*) 02.01.2003

D3: WO 2003/000708 A (Clontech Lab Inc) 03.01.2003

D4: WO 2004/055518 A1 (AstraZenica) 01.07.2003

D5: EP 972566 A2 (Tran Quang M) 19.01.2000

D6: US 5932102 A (Wyllie *et al.*) 03.08.1999

D7: US 2004/0112832 A1 (Sundberg et al.) 17.06.2004

D8: US 5384265 A (Kidwell *et al.*) 24.01.1995

D9: WO 2003/042249 A (Novo Nordisk) 22.05.2003

Novelty (N)

D1: defines a composition comprising an electrode comprising a covalently attached binding ligand that will bind a target analyte and a covalently attached solvent accessible transition metal complex comprising a metal selected from a group which includes ruthenium. The method defined comprises binding an analyte to a binding ligand that is either associated with or near to a transition metal complex. The transition metal complex is bound to an electrode through the use of a conductive oligomer. D1 is therefore novelty destroying for claims 1, 4, 5, 10, 20, 25, 26, 27.

D2: D2 defines a method for binding proteins to a substrate which comprises a ligand that can bind to a metal ion to form a chelator which is then chelated to a metal ion to form a metal-chelated substrate. The proteins are bound to the metal-chelated substrates by histidine residues that can bind to the available cis valences on the chelated metal ion. The protein is bound in an active form allowing it to perform native functions, and can be proteins such as antibodies (Page 2, Column 1) which will then be able to bind complementary antigens. The invention as claimed in claims 1-3, 6, 10, 11, 12, 20, 21, 25 and 26 is therefore not novel.

D3: D3 defines a method where a water soluble metal ion affinity compound and an analyte are immobilised on a solid support, such that during the contact step one of the complexes is immobilised on the solid support and the other is immobilised by virtue of binding to the solid support immobilised component. It is stated that it can be the metal ion affinity compound that initially binds to the solid support. Analytes may include un modified targets such as phosphorylated proteins. Claims 1, 22 and 25 are therefore not novel in the light of D3

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2005/000966

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

It is not clear in claims 1-29 as to whether the terms 'in the presence of a metal complex' includes the complex merely being in the solution with the target, or if the metal target can be bound the substrate or either of the two. As this issue is not clear the phrase has been taken in include all of these options.

It is also not clear in claims 1-24 as to whether the 'substrate' needs to be immobilised or not. It has been assumed that the substrate may be a stationary substrate, a substrate in solution or be either solid or not.

In order to conduct the search it is understood that it is an inherent property that the metal complexes would provide a stable binding interaction between a target molecule and the substrate when integral in binding the two.

The meaning of terms such as 'facilitate efficient binding', 'facilitate binding', 'control binding' and 'control total binding affinity' are not clear and do not appear to add any features to the scope of the claims.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: V

D4: D4 defines a method involving detecting inositol phosphate by contacting it with a metal immobilised to a substrate. The inositol is consequently immobilized through binding to the immobilised metal. D4 is novelty destroying for claims 1, 25 and 26.

D5: D5 defines a method of immobilizing a protein by contacting the protein to a resin which is coordinated to a metal ion. The protein is immobilized on the metal ion-resin complex. D5 is novelty destroying for claims 1, 25 and 26.

D6: D6 defines the use of a Zn resin (Metal complex) to bind an unmodified analyte via the native histamine residues in the analyte to the metal complex. Claims 1, 11,12, 25 and 26 are not novel in the light of D6.

D7: D7 defines a method of using metal ion affinity chromatography where polypeptides or endotoxins in solution are applied to a resin complexed with a metal, the targets (polypeptides or endotoxins) bind to the metal resin complex and are immobilised. D7 therefore discloses the features of claims 1, 25 and 26.

Inventive Step (IS)

D1: Claims 1, 4, 5, 10, 20, 25, 26, 27 lack and inventive step for reasons as stated above. Furthermore claims 2, 6, 9 and 21 lack and inventive step over D1 as it would require only routine steps to arrive at the solution of immobilising a complementary binding molecule using certain coordination ligands bound to a metal such as ruthenium (III) chloride.

D2: Claims 1-3, 6, 10, 11, 12, 20, 21, 25 and 26 lack an inventive step over D2 for reasons as stated above. Claims 17-19 also lack an inventive step as D1 teaches the use of a substrate modifier which with only routine steps may form a coating on a substrate.

D3: Claims 1, 22 and 25 lack an inventive step in the light of D3 for reasons stated above. Claims 2, 6 and 21 lack and inventive step over D3 as it would require only routine steps to arrive at the solution of immobilising a complementary binding molecule using specific coordination ligands associated with the metal complexes. Further more claims 17-19 lack an inventive step as the citation teaches of the use of linkers to bind the metal complexes to the substrate, these linkers could be used by a person skilled in the art as a coating on the substrate.

D4: Claims 1, 25 and 26 lack an inventive step for reasons stated above.

D5: Claims 1, 25 and 26 lack an inventive step for reasons stated above. Further more claims 2, 6 and 21 lack an inventive step in the light of D5 as it would require only routine steps to arrive at the solution of immobilising a complementary binding molecule using specific coordination ligands associated with the metal complexes.

D6: Claims 1, 11,12, 25 and 26 lack an inventive step in light of D6 for reasons stated above.

D7: Claims 1, 25 and 26 lack an inventive step in light of D7 for reasons stated above.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International Application No.

PCT/AU2005/000966

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: **V**

D8: D8 defines a method for detecting an analyte in a sample, comprising:

(i) contacting a sample which may contain an analyte with a biomolecule which is bonded to a catalytically active colloidal metal particle, said biomolecule being a specific binding complement of said analyte, to obtain an analyte-biomolecule-colloidal metal particle complex;

(ii) separating said analyte-biomolecule-colloidal metal particle complex from said sample;

(iii) contacting said analyte-biomolecule-colloidal metal particle complex with a substrate which forms a product in a reaction catalyzed by the colloidal metal particle of said complex; and

(iv) detecting said analyte-biomolecule-colloidal metal particle complex by detecting said product produced by a reaction of said substrate by the colloidal metal particle of said complex to indicate the presence or absence of said analyte in the sample,

wherein said colloidal metal particle comprises a metal selected from the group consisting of platinum, palladium, silver and mixture thereof; and said biomolecules is selected from the group consisting of antibodies, antigens, avidin, streptavidin, biotin, proteins bonded to a hapten, and nucleic acids.

D8 differs from the current invention in that the target molecule and metal complex are bound to a substrate, it would not require any inventive faculty and only routine steps to bind such complexes to a substrate and arrive at the solution of the current invention. Therefore Claims 1-3, 10-11 and 21 lack an inventive step.

D9: D9 defines the use and preparation of a functionalised polymer substrate which comprises a metal ion coordinated to at least one of the cyclic groups of the polymer. This functionalised polymer is contacted with a solution containing a target molecule which binds to the metal ion. This metal may be chromium.

D9 differs from the current invention in that the target molecules are not necessarily unmodified, however it would take only routine steps to arrive at the current solution of claims 22 and 23.